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| EXAMINER | |
|---|---|
| AEDER, SEAN E | |
| ART UNIT | PAPER NUMBER |
| 1642 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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| 3 MONTHS | 01/09/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,031 | GUELLY ET AL. | |
| | Examiner | Art Unit | |
| | Sean E. Aeder, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *22,23,27-33 and 47-84* is/are pending in the application.

4a) Of the above claim(s) *22,23,27-33,47-65,68 and 81-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66,67 and 69-80* is/are rejected.

7)☒ Claim(s) *73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Detailed Action***

The Amendments and Remarks filed 11/13/06 in response to the Office Action of 7/12/06 are acknowledged and have been entered.

Claims 66-84 have been added by Applicant.

Claims 22, 23, 27-33, 47-84 are pending.

Claims 22, 23, 27-33, 47-65, 68, and 81-84 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention. It further noted that claims 68 and 81 are withdrawn for not reading on diagnosing the elected species of hepatocyte carcinoma; rather, claims 68 and 81 are drawn to detecting unelected cancers of the lung, stomach, kidney, colon, prostate, skin, and breast. It is further noted that claims 81-84 are drawn to the unelected invention of group II.

Claims 66, 67 and 69-80 are currently under examination.

The text of those sections of Title 35 U.S.C. code not included in this Office Action can be found in a prior Office Action.

Further, it is noted that amended claims 66, 67, and 69-80 encompass unelected inventions drawn to detecting sequences other than SEQ ID NO:11 (methods of detecting unelected sequences SEQ ID NO:12-19). As noted in the Restriction Requirement of 4/10/06, each sequence represents a separate invention and not a species.

Further, it is noted that amended claims 66, 67, and 69-80 are drawn to unelected species of "ailments", "methods of detection", "methods of comparing", "samples from a patient" and "reference samples".

The following Office Action contains NEW GROUNDS of rejections Necessitated by Amendments which cancelled all previously pending claims.

## Objections

Claim 73 is objected to for reciting: "The method according to claim 70, wherein in step (1) the expression of said polynucleotide(s) is compared by a method selected from the group consisting of solid-phase based screening methods, hybridization, subtractive hybridization, differential display, and RNAase protection assay". Solid-phase based screening methods, hybridization, subtractive hybridization, differential display, and RNAase protection assay are not comparison methods. Rather, solid-phase based screening methods, hybridization, subtractive hybridization, differential display, and RNAase protection assay are detection methods. Proper correction is required.

## *New Rejections Necessitated By Amendments*

### *35 USC § 112, second paragraph*

Claims 66, 67 and 70-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 66 and dependent claim 67 are rejected because claim 66 recites: "...comparing expression of the polynucleotide(s) identified in step (1) with expression of said polynucleotide in a reference library or a reference sample from a non-diseased control, wherein over-expression of the identified polynucleotide(s) as compared to the reference library or reference sample is indicative of a diagnosis of liver disorder or epithelial cancer.". It is unclear how over-expression of the identified polynucleotide(s) as compared to the reference library or reference sample is indicative of a diagnosis of hepatocyte carcinoma. It is unclear whether over-expression of the identified polynucleotide(s) in a biological sample as compared to the reference library or reference sample indicates that the patient from which the biological sample was derived has hepatocyte carcinoma *or* whether over-expression of the identified polynucleotide(s) in a biological sample as compared to the reference library or reference sample indicates that the patient from which the biological sample was derived does not have hepatocyte carcinoma.

Claim 70 and dependent claims 71-80 are rejected because claim 70 recites: "...the reference sample". There is insufficient antecedent basis for this limitation in the claim.

Claim 70 and dependent claims 71-80 are rejected because claim 70 recites: "...matching said polynucleotide(s) identified in step (3) with said polynucleotide(s)

differentially expressed in a pathologic reference sample or pathologic reference library from a diseased control, wherein the matched polynucleotide(s) is (are) indicative of a diagnosis of liver disorder or epithelial cancer." It is unclear how said polynucleotides are to be "matched" or what kind of "match" would be indicative of hepatocyte carcinoma. There appear to be missing steps comprising comparing and correlating some kind of comparison to hepatocyte carcinoma. See MPEP 2172.01.

***Claim Rejections - 35 USC § 112***

Claims 66, 67, and 70-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing hepatocellular carcinoma in a patient comprising comparing the expression level of a polynucleotide comprising the sequence set forth in SEQ ID NO:11 in a first blood sample from said patient with the expression level of said polynucleotide in a second corresponding blood sample from a subject known to be free of hepatocellular carcinoma wherein elevated expression of SEQ ID NO:11 in the first blood sample as compared to the second blood sample indicates that the patient from which the first sample derived does not have metastatic hepatocellular carcinoma, the specification does not reasonably provide enablement for a method of diagnosing every liver disorder and every epithelial cancer in a patient wherein expression of SEQ ID NO:11 in just any type of patient sample is compared to just any type of sample or just of any type of reference library or of any other sample. Further, the specification is not enabling for a method of diagnosing every liver disorder and every epithelial cancer comprising

comparing the expression level of SEQ ID NO:11 polynucleotide in a sample from a patient with the expression of SEQ ID NO:11 polynucleotide in just any reference library or any reference sample and somehow "matching" nucleic acids that are differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample with nucleic acids differentially expressed in any type of pathologic reference sample or any type of pathologic reference library wherein "matched" nucleic acids are indicative of the patient suffering from every kind of liver disorder and every kind of epithelial cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are drawn to a method of diagnosing every liver disorder and every epithelial cancer in a patient wherein a polynucleotide comprising SEQ ID NO:11 is "identified" in any type of sample and "compared" with expression of a polynucleotide comprising SEQ ID NO:11 in just any reference library or reference sample from a non-diseased control, wherein overexpression of polynucleotides comprising SEQ ID NO:11

is "indicative of" a diagnosis of liver disorder or epithelial cancer (see independent claim 66). The claims are further drawn to a method of diagnosing every liver disorder and every epithelial cancer in a patient comprising detecting expression of a polynucleotide comprising SEQ ID NO:11 in any type of patient sample, comparing said expression to expression of said polynucleotide in some kind of reference library or some kind of reference from some kind of control, identifying polynucleotides which are differentially expressed between the patient sample as compared to said polynucleotides in the reference library or reference sample, and somehow "matching" nucleic acids that are differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample with nucleic acids differentially expressed in any type of pathologic reference sample or any type of pathologic reference library wherein "matched" nucleic acids are indicative of the patient suffering from every kind of liver disorder and every kind of epithelial cancer (see independent claim 70).

The specification prophetically discloses a method for diagnosing hepatocellular carcinoma in a patient comprising comparing the expression level of a polynucleotide comprising the sequence set forth in SEQ ID NO:11 in a first blood sample from said patient with the expression level of said polynucleotide in a second corresponding blood sample from a subject known to be free of hepatocellular carcinoma (Example 6, in particular). The instant specification does not demonstrate that expression of polynucleotides comprising SEQ ID NO:11 are elevated in *blood* of individuals with hepatocyte carcinoma.

Horne et al teaches a polynucleotide sequence, Sequence #2645, which consists of a 176 base pair polynucleotide sequence that shares 95.6% homology with 176 consecutive base pairs of instant SEQ ID NO:11 (see attached sequence comparison). Because of the high degree of homology of Sequence #2645 to a region of instant SEQ ID NO:11, one of skill in the art would recognize that reagents used to identify Sequence #2645, including polynucleotide complements of Sequence #2645, would detect polynucleotides comprising instant SEQ ID NO:11.. Horne et al further teaches a method of diagnosis of hepatocellular carcinoma wherein expression of a polynucleotide comprising SEQ ID NO:11 would be identified in a blood sample from a patient and compared with expression of a polynucleotide comprising SEQ ID NO:11 in a reference library or a reference blood sample from a non-diseased control, wherein overexpression of polynucleotides comprising SEQ ID NO:11 in the blood sample from the patient is indicative of a diagnosis of hepatocyte carcinoma wherein said diagnosis is that patient from which the sample was derived does not have metastatic hepatocellular carcinoma (page 11 lines 20-33, in particular). Further, Horne et al teaches a method of diagnosing hepatocellular carcinoma comprising the following steps: (a) detecting the expression of a polynucleotide comprising SEQ ID NO:11 in a blood sample isolated from a patient, (b) comparing said expression with the expression of polynucleotides comprising SEQ ID NO:11 in a reference library or in a reference blood sample, (c) identifying polynucleotides which are differentially expressed between the blood sample isolated from the patient as compared to the reference library or the reference blood sample, and (d) matching said nucleic acid(s) identified in step (c) with

said nucleic acid(s) differentially expressed in a pathologic reference blood or sample or pathologic reference library, wherein the matched nucleic acid(s) is (are) indicative of the patient of a diagnosis wherein said diagnosis is that patient from which the sample was derived does not have metastatic hepatocellular carcinoma (page 11 lines 20-33, in particular).

The state of the prior art dictates that if a molecule such as the polynucleotide set forth in SEQ ID NO:11 is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with

subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the polynucleotide's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the polynucleotide in any diagnostic setting without undue experimentation.

The level of unpredictability for the detection of any disease is quite high. Since neither the specification nor the prior art provide evidence of a universal association between the claimed method of detecting the polynucleotide set forth in SEQ ID NO:11 and every type of ailment and using every type of sample and every type of reference, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn a method of diagnosing every liver disorder and every epithelial cancer in a patient wherein a polynucleotide comprising SEQ ID NO:11 is "identified" in any type of sample and "compared" with expression of a polynucleotide comprising SEQ ID NO:11 in just any reference library or reference

sample from a non-diseased control, wherein overexpression of polynucleotides comprising SEQ ID NO:11 is "indicative of" a diagnosis of liver disorder or epithelial cancer, and Applicant has not enabled said method because it has not been shown that overexpression of polynucleotides comprising SEQ ID NO:11 in just any type of sample would predictably diagnose every type of liver disorder and every type of epithelial cancer. Further, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method of diagnosing every liver disorder and every epithelial cancer in a patient comprising detecting expression of a polynucleotide comprising SEQ ID NO:11 in any type of patient sample, comparing said expression to expression of said polynucleotide in some kind of reference library or some kind of reference from some kind of control, identifying polynucleotides which are differentially expressed between the patient sample as compared to said polynucleotides in the reference library or reference sample, and somehow "matching" nucleic acids that are differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample with nucleic acids differentially expressed in any type of pathologic reference sample or any type of pathologic reference library wherein "matched" nucleic acids are indicative of the patient suffering from every kind of liver disorder and every kind of epithelial cancer, and Applicant has not enabled said method because it has not been shown that detecting expression nucleic acids comprising SEQ ID NO:11 in every type of sample from a patient and comparing the expression of said nucleic acid with the expression of said nucleic acid in just any reference library or any reference sample and somehow

"matching" nucleic acids that are differentially expressed in the sample isolated from the patient compared to the reference library or the reference sample with nucleic acids differentially expressed in any type of pathologic reference sample or any type of pathologic reference library wherein "matched" nucleic acids are predictably indicative of the patient suffering from every kind of liver disorder and every kind of epithelial cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66, 67 and 69-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Horne et al (WO 02/29103 A2; 4/11/02).

Claims 66-67 are drawn to a method of diagnosing hepatocyte carcinoma in a patient wherein a polynucleotide comprising SEQ ID NO:11 is "identified" in a blood sample and "compared" with expression of a polynucleotide comprising SEQ ID NO:11 in a reference library or reference blood sample from a non-diseased control, wherein

overexpression of polynucleotides comprising SEQ ID NO:11 is "indicative of" a diagnosis of hepatocyte carcinoma. Claim 69 is drawn to a method comprising detecting expression of a polynucleotide comprising SEQ ID NO:11 in a blood sample from a patient and comparing expression of said polynucleotide in said blood sample from a patient with expression of said polynucleotide in a reference library or in a reference and identifying said polynucleotide which is differentially expressed in said blood sample from a patient as compared to said polynucleotide in the reference library or reference blood sample. Claims 70, 74, 76, and 80 are drawn to a method of diagnosing hepatocyte carcinoma in a patient comprising detecting expression of a polynucleotide comprising SEQ ID NO:11 in a blood sample, comparing said expression to expression of said polynucleotide in some kind of reference library or some kind of reference from some kind of control, identifying polynucleotides which are differentially expressed between the patient blood sample as compared to said polynucleotides in the reference library or reference blood sample, and somehow "matching" nucleic acids that are differentially expressed in the blood samples that are isolated from the patient compared to the reference library or the reference blood sample with nucleic acids differentially expressed in any type of pathologic reference sample or any type of pathologic reference library wherein "matched" nucleic acids are indicative of the patient suffering from hepatocyte carcinoma. Claim 71 is drawn to the method of claim 70, wherein at least 2 polynucleotides are identified during the detection of polynucleotides comprising SEQ ID NO:11. Claim 72 is drawn to the method according to claim 70, wherein detection of polynucleotides comprising SEQ ID NO:11 is performed by PCR

based detection or by hybridization assay. Claim 73 is drawn to the method according to claim 70, wherein the expression of polynucleotides comprising SEQ ID NO:11 is compared by a method selected from the group consisting of solid-phase based screening methods, hybridization, subtractive hybridization, differential display, and RNase protection assay. Claim 75 is drawn to the method of claim 70, wherein the reference sample is isolated from a source selected from non-diseased sample of the same patient and a non-diseased sample from another subject. Claim 77 is drawn to the method of claim 70, wherein the reference library is an expression library or a data base comprising clones or data on liver disorder-specific expression of nucleic acids comprising SEQ ID NO:11. Claim 78 is drawn to the method according to claim 70, wherein the pathologic reference sample is isolated from a source selected from a diseased sample from another patient suffering from a liver disorder or epithelial cancer. Claim 79 is drawn to the method of claim 70, wherein the pathologic reference library is a data base comprising data on differential expression of polynucleotides comprising SEQ ID NO:11 in samples isolated from another patient suffering from hepatocyte carcinoma relative to control expression in a reference sample or reference library.

Horne et al teaches a polynucleotide sequence, Sequence #2645, which consists of a 176 base pair polynucleotide sequence that shares 95.6% homology with 176 consecutive base pairs of instant SEQ ID NO:11 (see attached sequence comparison). Because of the high degree of homology of Sequence #2645 to a region of instant SEQ ID NO:11, one of skill in the art would recognize that reagents used to identify Sequence #2645, including polynucleotide complements of Sequence #2645, would

detect polynucleotides comprising instant SEQ ID NO:11. Horne et al further teaches a method of diagnosis of hepatocellular carcinoma wherein expression of a polynucleotide comprising SEQ ID NO:11 would be identified in a blood sample from patient and compared with expression of a polynucleotide comprising SEQ ID NO:11 in a reference library or a reference blood sample from a non-diseased control, wherein overexpression of polynucleotides comprising SEQ ID NO:11 is indicative of a diagnosis of hepatocyte carcinoma (page 11 lines 20-33, in particular). Further, Horne et al teaches a method of diagnosing hepatocellular carcinoma comprising the following steps: (a) detecting the expression of a polynucleotide comprising SEQ ID NO:11 in a blood sample isolated from a patient, (b) comparing said expression with the expression of polynucleotides comprising SEQ ID NO:11 in a reference library or in a reference blood sample, (c) identifying polynucleotides which are differentially expressed between the blood sample isolated from the patient as compared to the reference library or the reference blood sample, and (d) matching said nucleic acid(s) identified in step (c) with said nucleic acid(s) differentially expressed in a pathologic reference blood or sample or pathologic reference library, wherein the matched nucleic acid(s) is (are) indicative of the patient suffering from a hepatocellular carcinoma (page 11 lines 20-33, in particular). Horne et al further teaches a method wherein said nucleic acids are detected by PCR based detection or by a hybridization assay (page 13, in particular). Horne et al further teaches a method wherein the expression of said nucleic acids are compared by a solid-phase based screening methods (page 19, in particular). Horne et al further teaches a method wherein the patient sample is blood (page 18 lines 25-30, in

particular). Horne et al further teaches a method wherein the reference sample is isolated from a source selected from a non-diseased blood sample from another subject (page 11 lines 20-33 and page 18 lines 25-30, in particular). Horne et al further teaches a method wherein the reference library is an expression library or a data base comprising clones or data on hepatocellular carcinoma-specific expression of SEQ ID NO:11 (pages 11, 21, and 22, in particular).

In the Reply of 11/13/06, Applicant argues that Horne et al fails to teach instant SEQ ID NO:11. Applicant indicates that failure to teach the exact sequence of instant SEQ ID NO:11 demonstrates that Horne et al doe not teach each and every element of the claimed invention. Applicant further argues that the polynucleotide sequence taught by Horne et al is disclosed to be down-regulated in metastatic malignant tumor (secondary liver cancer). Applicant argues that downregulation of the sequence taught by Horne et al is the opposite expression pattern compared to elected SEQ ID NO:11 of the present invention, which Applicant states is highly up-regulated in HCC (primary liver cancer). Applicant concludes that the sequence taught by Horne et al is not an optimal HCC biomarker, and it would not be used in the claimed method. Applicant states that one skilled in the art would not select the sequence taught by Horne et al because it is not an optimal HCC biomarker.

The arguments found in the Reply of 11/13/06 have been carefully considered, but are not deemed persuasive. In regards to the argument that Horne et al fails to teach instant SEQ ID NO:11, the pending claims are not drawn to a *product* comprising SEQ ID NO:11; rather, the pending claims are drawn to a *method* of identifying a

polynucleotide comprising SEQ ID NO:11. Due to the high degree of homology between the sequence taught by Horne et al and instant SEQ ID NO:11, one of skill in the art would recognize that complements of the sequence taught by Horne et al *would* identify instant SEQ ID NO:11. In regard to the argument that that downregulation of the sequence taught by Horne et al is the opposite expression pattern compared to elected SEQ ID NO:11 of the present invention, which Applicant states is highly up-regulated in HCC (primary liver cancer), the pending claims are not drawn to method wherein overexpression of a polynucleotide comprising SEQ ID NO:11 in a sample indicates that the patient from which the sample is derived has hepatocyte carcinoma. Rather, the claims are drawn to a method wherein overexpression of a polynucleotide comprising SEQ ID NO:11 in a sample is "indicative of a diagnosis" of hepatocyte carcinoma. The claims are not drawn to a *specific* diagnosis of hepatocyte carcinoma (see 112, second paragraph rejection above). Thus, Horne et al, which teaches SEQ ID NO:2645 is downregulated in hepatocyte carcinoma as compared to normal controls, teaches that overexpression of SEQ ID NO:11 is indicative of a diagnosis of hepatocyte carcinoma wherein the diagnosis is that a patient with greater expression in the biological sample, as compared to the controls, does not have hepatocyte carcinoma. Further, it is noted that limitations disclosed in the instant specification are not read into the pending claims.

***Summary***

No claim is allowed.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a). A shortened statutory period for response to this Final Action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this Final Action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. '1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than six months from the date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

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